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| EXAMINER | |
|---|---|
| KOLKER, DANIEL E | |
| **ART UNIT** | **PAPER NUMBER** |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/830,972 | SCHWAB ET AL. | |
| | Examiner | Art Unit | |
| | Daniel Kolker | 1649 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 June 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *114–119, 123-132,135–146* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *127-132* is/are allowed.

6)☒ Claim(s) *114-119,123-126 and 135-146* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/21/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

1. The remarks, amendments, and declaration filed 21 June 2007 have been entered. Claims 114 – 119, 123 – 132, and 135 – 146 are pending.

### *Withdrawn Rejections and Objections*

2. The following rejections and objections set forth in the previous office action are withdrawn:

A. The rejection of claims 136 and 141 under 35 USC 112, first paragraph for lack of adequate written description is withdrawn in light of the arguments. Applicant persuasively argues, on p. 17 of the remarks filed 21 June 2007, that the invention of claim 136 does not constitute new matter.

B. The examiner's concerns about the effective filing date of claims 136 and 141 (see section entitled Priority beginning at the bottom of page 11 of the office action mailed 21 December 2006) have been overcome. As set forth in the preceding paragraph, claims 136 and 141 do not recite new matter. As such, these claims and all other pending claims are entitled to an effective filing date of 6 November 1998.

C. The rejection of claims 127 and 138 under 35 USC 102(b) as anticipated by Chen (1997. Society for Neuroscience Abstracts 23:1723) is withdrawn in light of the arguments and declaration filed 21 June 2007. The declaration under 37 CFR 1.132 filed 21 June 2007 is sufficient to overcome the rejection of claims 127 and 138 based upon the argument that the Chen reference is not an enabling disclosure. Chen names three cDNA clones but does not disclose how to make them, nor does the reference disclose how to obtain Nogo protein sufficiently free of myelin such that the protein could be sequenced and oligonucleotide primers could be designed. As persuasively argued by applicant at p. 19 of the remarks and paragraph 46 of the declaration, and consistent with the guidance set forth in MPEP §§ 2121(III) and 2121.01, merely naming a product does not constitute an enabling disclosure in the prior art if the product cannot be made without undue experimentation. The declaration states (paragraph 46) that no sequence information was presented and that the clones were not made available to the public.

D. The rejection of claims 115 – 116, 118 – 119, 123 – 125, 127, 135 – 138, and 141 under 35 USC 103(a) as obvious over Chen (1997. Society for Neuroscience Abstracts 23:1723) in view of Sambrook (1989) is withdrawn in light of the arguments and declaration. As set forth in the previous paragraph, the Chen (1997) reference does not anticipate claims 127

and 138 therefore the artisan of ordinary skill would not have been motivated to modify the named cDNAs by inserting them in vectors and making protein.

E. The rejection of claims 114 – 119, 123 – 125, 135, 137, 139, and 141 under 35 USC 103(a) as obvious over Schwab (U.S. Patent 5,250,414) in view of Spillmann (1995) is withdrawn in light of the arguments and declaration. The declaration under 37 CFR 1.132 filed 21 June 2007 is sufficient to overcome the rejection of claims 114 – 119, 123 – 125, 135, 137, 139, and 141 based upon the arguments that the techniques to purify Nogo protein disclosed in both references were not sufficient to in fact purify the protein. In the declaration filed 21 June 2007, Dr. Schwab argues that the techniques described in Spillmann 1995 did not result in protein free of all myelin material as required by the claims (see paragraph 28). Dr. Schwab further argues that many non-obvious steps were required including selection of the appropriate buffer so that the cells used in the bioassays are not killed (declaration, paragraphs 31 – 34). Dr. Schwab states that a crucial step was finding a non-SDS buffer, as SDS denatures cell membranes. It is noted that Nogo protein is membrane-associated (declaration, paragraph 10). Additionally, the declaration states that the procedures detailed in Schwab '414 patent at columns 18, 42, 48, and 50 were not sufficient to purify the protein as required by the instant claims. Finally, the declaration mentions the failures of others in the field to purify the claimed proteins (paragraphs 11 – 13), which can be taken as evidence of non-obviousness; see MPEP § 2145. Taken as a whole, the declaration provides persuasive evidence that purification of the prior art product would not have been obvious to one of ordinary skill in the art.

### *Rejections Maintained and Necessitated by Amendment*

### *Claim Rejections - 35 USC § 112*

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 115 – 116, 118 – 119, 123 – 125, 135 – 136, and 138 – 146 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for full-length proteins and fusions proteins which inhibit spreading of NIH3T3 fibroblasts or PC12 cells (i.e. SEQ ID NO:2, SEQ ID NO:29, residues 1 – 171 of SEQ ID NO:2 fused to residues 975 – 1163 of SEQ ID NO:2, residues 1-172 of SEQ ID NO:29 fused to residues 990-1178 of SEQ ID NO:29) and proteins which have been shown in the specification to elicit antibodies which

attenuate the inhibitory effects of Nogo (i.e. residues 623-640 of SEQ ID NO:2 and residues 762-1163 of SEQ ID NO:2), does not reasonably provide enablement for those fragments claimed that do not inhibit fibroblast spreading, or for fragments which merely are able to elicit antibodies for which no in vitro or in vivo data have been provided, or for fragments which merely bind to certain antibodies, or nucleic acids which encode same. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

As a preliminary matter, the examiner notes that claim 135 was inadvertently omitted from the listing of rejected claims which appeared in the first paragraph of page 3 of the office action mailed 21 December 2006. However claim 135 was clearly included in the rejection, and discussed in detail at page 6 of that office action. Therefore, inclusion of claim 135 in the instant rejection does not constitute a new grounds of rejection. Additionally, it is noted that the inclusion of functional language in the first paragraph of claim 135 necessitates additional grounds of rejection.

This rejection stands for the reasons of record. Briefly, the specification does not disclose to the skilled artisan how to use those proteins (or nucleic acids encoding same; for the sake of simplicity the discussion here is limited to proteins, as the sole patentable utility for the nucleic acids is for making of proteins) whose only function is to generate an antibody or bind to an antibody. That is, elements (i) and (ii) of claims 115 – 116, 118 – 119, and 136, as well as elements (i) - (iv) of claim 135 and 138 are not enabled over their full scope. The claims include proteins that bind to antibodies but that themselves have no ability to inhibit spreading of PC12 cells or NIH3T3 cells. Elements (iii) – (vii) of claims 115— 116, and 118 – 119 are limited to proteins which in fact are useful in these assays, but the same is not true of the claim elements drawn to proteins whose only function is to generate or bind to antibodies.

Applicant argues, on 12 – 14 of the remarks filed 21 June 2007, that the specification provides several uses for proteins which generate antibodies and bind to antibodies but which have no ability to inhibit cell spreading or neurite outgrowth. The examiner disagrees with applicant's assertion of uses for the claimed proteins. The issue has been discussed at great length in the previous office actions and in applicant's responses to the office actions. The issue has been discussed with respect to the prior art of record, particularly the references by Hopp et al. and by Geysen et al. (both previously made of record). In the final analysis, applicant is claiming proteins but has not taught the public how to use those proteins. The proteins which are within the scope of claims 115 – 116, 118 – 119, 135 – 136, and 138 and

either bind to antibodies or generate antibodies but which themselves have no activity in inhibiting neurite outgrowth or cell spreading, do not meet the requirements of 35 USC § 112, first paragraph. This statute explicitly requires that the claimed invention show both how to make and how to use the claimed invention.

On p. 15 third paragraph of the remarks filed 21 June 2007, applicant states that when multiple uses for a product are disclosed, "any of the uses, such as the generation of antibodies, can support enablement." This statement is not consistent with the guidance set forth in MPEP § 2164.08. Applicant cites MPEP § 2164.01(c), which states in part that "if any use is enabled... the application is enabling for the claimed invention." While this is of course true, applicant is directed to the more relevant section of MPEP, which particularly deals with the question of whether or not enablement is *commensurate in scope with the claims*. See for example MPEP § 2164.08, which states:

> All questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether <u>everything</u> within the scope of the claim is enabled.... The Federal Circuit has repeatedly held that "the specification must teach those skilled in the art how to make and use <u>the full scope</u> of the claimed invention without undue experimentation'." In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). [emphasis added]

Here, what is enabled is considerably narrower in scope with what is claimed. The specification fails to provide adequate guidance as to how to use the full scope of the claimed invention. The skilled artisan would thus have to resort to a very large degree of experimentation to determine how to use those proteins which do not have the neurite-outgrowth-inhibiting or cell-spreading-inhibiting activities. Coupled with the paucity of guidance provided by the specification, this large degree of experimentation would be undue.

Applicant states, in the paragraph spanning pp. 15 – 16 of the remarks filed 21 June 2007, that claims 135 – 136 have been amended "to recite that the Nogo proteins have one or more specified functional activities." However, as detailed above, each of these claims encompass proteins whose only function is to bind to antibodies or to regenerate antibodies. Merely binding antibodies or generating antibodies is itself not useful, and such an assay does not define a distinguishable activity to enable the artisan to determine how to use the variants encompassed by claims 135 - 136. Additionally, as set forth at p. 6 second complete paragraph

of the office action mailed 21 December 2006, claim 35 encompasses SEQ ID NO:43 (see claim 35, element (ii)), which the specification does not disclose how to use. Similarly, claim 139 element (i) encompasses as 27 amino acid protein which the specification does not disclose how to use and which the skilled artisan would not know how to use in the absence of undue experimentation.

New claims 142 – 146 each depend from at least one rejected claims and therefore are rejected as well. The examiner notes that if applicant were to amend the claims such that the only activities of proteins claimed were those set forth as elements (iv) – (vii) of claim 115, the rejection would be withdrawn. However as applicant is claiming proteins which the specification does not disclose how to use, and for which undue experimentation would be required to determine how to use, the scope of enablement rejection stands.

4. Claims 115 – 116, 118 – 119, 123 – 125, 136, 138, 141, and 142 – 146 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

This rejection stands for the reasons previously made of record with respect to claims previously rejected (i.e. claims 115 – 116, 118 – 119, 123 – 125, 136, 138, 141) and is expanded to new claims 142 – 146, which depend from at least one rejected claim as well. Applicant states that the previous responses had provided known structure-function correlations (see remarks filed 21 June 2007, p. 16 final paragraph). As set forth previously, there is not sufficient correlation between the structures described (i.e. those at least 95% identical to disclosed residues) and functions claimed (i.e. generating or binding to antibodies) to allow the skilled artisan to visualize the claimed proteins and nucleic acids. The specification does not describe which elements are common to all members of the claimed genera. The specification fails to describe which 95% of the sequences are retained such that the claimed functions are necessarily present. The specification fails to disclose which 5% of the sequences can or should be altered or deleted without impeding the claimed functions. As there is not sufficient correlation between structure and function of the claimed proteins and nucleic acids, they have not been described.

***Double Patenting***

5. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 114 – 119, 123 – 126, 135, 137, 139, 141, and 145 - 146 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 2 – 3 of U.S. Patent No. 5,684,133 (cited on IDS filed 19 March 2003). Although the conflicting claims are not identical, they are not patentably distinct from each other because in both cases the claims encompass the proteins now referred to as "Nogo-A". In the '133 patent they are not referred to by this name, but the proteins are disclosed as being 250 kD (note claims 2 – 3 from the '133 patent are generic with respect to molecular weight) and in both cases they have ability to inhibit neurite outgrowth and are bound by antibodies IN-1 and IN-2. Furthermore, the proteins of claims 2 – 3 of the '133 patent are "essentially purified and isolated", which is not patentably distinct from "free of all central nervous system myelin material" as now claimed. Note claims 145 – 146 are included in this rejection as they are product-by-process claims. The

products encompassed by these claims are patentably indistinct from the claims in the '133 patent, as in each case they are "essentially purified and isolated".

Applicant argues, at p, 31 of the remarks filed 21 June 2007, that the double-patenting rejection is improper because the instant claims are not obvious over any disclosed prior art. Applicant argues that MPEP § 804(II)(B)(I) instructs examiners to employ an obviousness analysis parallel to that which would be used in considering rejections under 35 USC § 103. Applicant's arguments have been fully considered but they are not persuasive. The section of MPEP cited by applicant applies only to those cases where the invention is not anticipated by a claim in an issued patent, but rather is a variant of an issued claim. The full text states that:

> A double patenting rejection of the obviousness-type, if not based on an anticipation rationale, is "analogous to [a failure to meet] the nonobviousness requirement of 35 U.S.C. 103" except that the patent principally underlying the double patenting rejection is not considered prior art. In re Braithwaite, 379 F.2d 594, 154 USPQ 29 (CCPA 1967). Therefore, the analysis employed in an obviousness-type double patenting rejection parallels the guidelines for analysis of a 35 U.S.C. 103 obviousness determination. [emphasis added]

However, such analysis does not apply when the issued claims anticipate claims in an application. Claims 2 – 3 of the '133 patent are drawn to "An essentially purified and isolated neurite growth inhibitory factor consisting of a protein" which has certain properties that are indistinguishable from those of the claims subject to this rejection. The issued claims anticipate the pending claims, so the double-patenting rejection is appropriate. The claims in issued patents enjoy the presumption of validity, and are drawn to "essentially purified and isolated" proteins.

***Conclusion***

6. Claims 127 – 132 are allowed.

7. Claims 114 - 119, 123 – 126, and 135 –146 are rejected.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Daniel Kolker whose telephone number is (571) 272-3181. The examiner can normally be reached on Mon - Fri 8:30AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker can be reached on (571) 272-0911. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

DK

Daniel E. Kolker, Ph.D.
January 4, 2008

ROBERT C. HAYES, PH.D.
PRIMARY EXAMINER